CLAIMS

We claim:

1. Extruded-spheronized beadlets comprising stavudine, a spheronizing agent, and a quantity of magnesium stearate sufficient to stabilize stavudine against degradation during the extrusion-spheronization process.

2. The beadlets of with Claim 1 containing from about 0.5 to about 3.0 percent by weight of magnesium stearate based on the weight of stavudine present therein.

3. The beadlets of with Claim 1 containing from about 1.4 to about 1.7 percent by weight of magnesium stearate based on the weight of stavudine present therein.

4. The beadlets of Claim 1 wherein the spheronizing agent is selected from the group consisting of microcrystalline cellulose, sodium carboxymethyl cellulose and corn starch.

5. The beadlets in Claim 4 wherein the spheronizing agent is microcrystalline cellulose.

6. The beadlets of Claim 1, further comprising a diluent.

7. The beadlets of Claim 6 wherein said diluent is selected from consisting of lactose, dicalcium phosphate, mannitol and cornstarch.

8. The beadlets of Claim 1, further comprising a seal coating and a modified release coating.

9. The beadlets of Claim 8 wherein the said seal coating comprises a film-former and an antiadherent, and the modified release coating comprises a polymeric barrier material and a plasticizer therefor.

10. The beadlets of Claim 9 wherein the film former is selected from the group consisting of hydroxypropylmethylcellulose and dydroxypropylcellulose.

11. The beadlets of Claim 9 wherein the antiadherent is selected from the group consisting of talc, microcrystalline cellulose and magnesium stearate.

12. The beadlets of Claim 9 wherein the polymeric barrier material comprises polymethacrylate.

13. The beadlets of Claim 9 wherein the polymeric barrier material comprises ethylcellulose.

14. The beadlets of Claim 9 wherein the plasticizer comprises acylated monoglycerides.

15. Extended-sphereonized beadlets, comprising:

a) stavudine;

b) a spheronizing agent;

c) a diluent;

d) magnesium stearate in an amount sufficent to stabilize stavudine against degredation during the extrusion-spheronization process;

e) a seal coating; and

f) a modified release coating.

16. The beadlets of Claim 15 containing from about 33 to about 67 percent by weight of stavudine.

17. The beadlets of Claim 15 wherein the spheronizing agent is selected from the group consisting of microcrystalline cellulose, sodium carboxymethyl cellulose and corn starch.

18. The beadlets of Claim 15 wherein the diluent is selected from the group consisting of lactose, dicalcium phosphate, manitol and corn starch.

19. The beadlets of Claim 15 wherein
a) the spheronizng agent is microcrystalline cellulose;
b) the diluent is lactose;
c) the seal coating comprises a film former and an antiadherent; and
d) the modified release coating comprisese a polymeric barrier material and a plasticizer.

20. The beadlets of with Claim 19 wherein said film-former is hydroxypropyl methylcellulose, said antiadherent is talc, said polymeric barrier material is ethylcellulose and said plasticizer comprises distilled acetylated monoglycerides.

21. The pharmaceutical dosage form comprising a hard gelatin capsule containing a sufficient amount of the beadlets of Claim 1, 15 or 19 to provide an effective dosage of stavudine over approximately 24 hours.

22. The pharmaceutical dosage form of Claim 21, wherein said capsule additionally contains beadlets containing at least one other medicament useful in treating retroviral infections such that blood levels of said at least one other medicament are provided over approximately 24 hours.

23. A pharmaceutical dosage form of Claim 22, wherein said other medicaments are selected from the group consisting of didanosine, [3S-(3R*,8R*,9R*,12R*)]-3,12-Bis(1,1-dimethylethyl)-8-hydroxy-4,11-dioxo-9-(phenylmethyl)-6{[4-(2-pyridinyl)phenyl]methyl}-2,3,6,10,13-pentaazaretetradecanedioic acid dimethyl ester, indinavir and lodenosine.

24. The pharmaceutical dosage form of Claim 23 wherein said at least one other medicament is didanosine.

25. The pharmaceutical dosage form Claim 24 wherein said other medicament comprises
(a) [3S-(3R*,8R*,9R*,12R*)]-3,12-Bis(1,1-dimethylethyl)-8-hydroxy-4,11-dioxo-9-(phenylmethyl)-6{[4-(2-pyridinyl)phenyl]methyl}-2,3,6,10,13-pentaazaretetradecanedioic acid dimethyl ester; and
(b) an optional further medicament selected from the group consisting of didanosine and [3S-(3R*,8R*,9R*,12R*)]-3,12-Bis(1,1-dimethylethyl)-8-hydroxy-4,11-dioxo-9-(phenylmethyl)-6{[4-(2-pyridinyl)phenyl]methyl}-2,3,6,10,13-pentaazaretetradecanedioic acid dimethyl ester.

26. A method of treating a patient in need of therapy for a retroviral infection comprising administering to said patient a pharmaceutical dosage form comprising a hard gelatin capsule containing a sufficient amount of the beadlets of Claim 1, 15 or 19 to provide an effective dosage of stavudine, thereby providing said treatment over approximately 24 hours.

27. The method of Claim 26 wherein said capsule additionally contains beadlets containing at least one other medicament useful in treating retroviral infections such that treatment with said at least one other medicament is provided over approximately 24 hours.

28. The method Claim 27 wherein said at least one other medicament is selected from the group consisting of didanosine, [3S-(3R*,8R*,9R*,12R*)]-3,12-Bis(1,1-dimethylethyl)-8-hydroxy-4,11-dioxo-9-(phenylmethyl)-6{[4-(2-pyridinyl)phenyl]methyl}-2,3,6,10,13-pentaazaretetradecanedioic acid dimethyl ester, indinavir and lodenosine.

29. The method of Claim 28 wherein said other medicament is at least one of didanosine and [3S-(3R*,8R*,9R*,12R*)]-3,12-Bis(1,1-dimethylethyl)-8-hydroxy-4,11-dioxo-9-(phenylmethyl)-6{[4-(2-pyridinyl)phenyl]methyl}-2,3,6,10,13-pentaazaretetradecanedioic acid dimethyl ester.

30. The method of Claim 29 wherein said other medicament is didanosine.

31. A process of forming beadlets containing stavudine, comprising:
(a) forming a wet mass of stavudine, a spheronizing agent, an optional diluent, an amount of magnesium stearate sufficient to stabilize the stavudine against degradation during said process, and water sufficient to form a wet mass suitable for extrusion;
(b) extruding said mass to form an extrudate, spheronizing said extrudate;
(c) to form beadlets and drying said beadlets.

32. The process of Claim 31, further comprising the steps of forming a seal coating over said beadlets and forming a modified release coating over said seal coating.

33. The process of Claim 32 wherein said spheronizing agent is microcrystalline cellulose, said diluent is lactose, said seal coating comprises a film-former and an antiadherent, and said modified release coating comprises a polymeric barrier material and a plasticizer therefor.

34. The process of Claim 31, futher comprising the step of blending stavudine, the spheronizising agent, the optional diluent and magnesium stearate prior to forming the wet mass.